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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,264	12/08/2004	Andrea Mahn	4121-168	9836

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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EXAMINER	
WORLEY, CATHY KINGDON	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 09/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,264	MAHN ET AL.	
	Examiner	Art Unit	
	Cathy K. Worley	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *2,3,5-8,12,14 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,9-11,13 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction/Election

1. In response to the communication received on June 16, 2006 from Steven J. Hultquist, the Examiner acknowledges the election with traverse of the invention of a method of increasing the content of one or more transgene-coded biomolecules in an organism, the method comprising changing the distribution of ATP and/or ADP in cells of the organism, wherein:

a) the transgene is regulated in a constitutive manner;

b) several transgene biomolecules are expressed in parallel;

c) the host organism is a plant;

d) the transgene encodes a protein;

e) the transgene encodes an antibody;

f) the activity or concentration of protein involved in the subcellular distribution of ATP and/or ADP is decreased (this is implied by the election in part "g");

g) expression of a gene which codes for a protein involved in the subcellular distribution of ATP and/or ADP is decreased;

and

h) the expression of a gene which codes for a protein involved in the subcellular distribution of ATP and/or ADP is constitutive.

The Applicant points out that the elements listed in part "f" of the restriction requirement do not apply to the claimed invention (see part "f" on page 6 of the

response received on June 16, 2006). The Examiner thanks the Applicant for pointing out this error. The Examiner intended to include "the activity or concentration of protein involved in the subcellular distribution of ATP and/or ADP is either increased or decreased", and made an error in drafting the action. The Examiner believes that "decreased" is the choice that is consistent with the elected invention of part "g". If this is in error, then the Applicant is invited to correct the Examiner.

The Applicant argues that the restriction between methods with different regulation of the transgene or the ATP/ADP transporter (constitutive, temporally, locally, or inducibly: parts "a" and "h" of the restriction requirement) should be withdrawn because the novelty of the invention is achieved regardless of the kind of regulation of expression (see second paragraph on page 7 of the response). The Applicant further argues that the restriction between expressing in parallel or sequentially should be withdrawn for the same reason (see second paragraph on page 7 of the response). These arguments are found persuasive, and therefore, the Examiner will withdraw the restriction between the inventions having unique combinations of elements listed in parts "a", "b", and "h" of the restriction requirement.

The Applicant argues that the restriction between the peptide and protein in part "d" should be withdrawn because the peptide and protein have the same chemical structure (see part "d" on page 6 of the response). This is found to be

persuasive, and therefore the restriction between the peptide and the protein; however, the restriction between the nucleic acid and protein/peptide is not withdrawn.

The Applicant further argues that the restriction requirement between the class of biomolecules (part "e" of the restriction requirement) should be withdrawn because the novelty of the invention is achieved regardless of the kind of biomolecule being expressed (see second paragraph on page 7 of the response). This is found to be persuasive for those biomolecules that are proteins or peptides, therefore, the restriction between the different proteins is withdrawn. However, this is not found to be persuasive for the non-protein bio-molecules (aptamers, ribozymes, and other nucleic acids).

The Applicant refers to their response as an "election of species" (see page 6 of the response), and this is not correct. Each of the unique combinations of elements were independent inventions rather than species of a broader genus (see the last paragraph on page 2 of the previous Office Action mailed on May 16, 2006).

Therefore, claims that read on a method comprising a decrease in a protein involved in ATP/ADP distribution in a plant that leads to an increase in a protein or peptide encoded by a transgene will be examined. The Applicant is advised to amend all claims to read only on the elected invention.

Claim 12 is drawn to a method wherein the expression of an ATP/ADP transporter is increased, therefore it is withdrawn from consideration because it is

drawn to a non-elected invention. Claims 2-3, 5-8 and 14 depend from claim 12, therefore, they are also withdrawn from consideration. Claims 16-19 are drawn to expression of a plastidiary ATP/ADP transporter protein, therefore this is an increase rather than a decrease in a protein involved in ATP/ADP distribution, and it is a non-elected invention. Claim 1-19 are pending and claims 2-3, 5-8, 12, 14, and 16-19 are withdrawn from consideration.

Specification

2. The abstract of the disclosure is objected to because it is not descriptive enough of the invention. The abstract should be between 50 and 150 words in length and it should describe the elected invention. In the instant application, the abstract should specify that antisense suppression of an ATP transporter in a transgenic plant is utilized to cause in increase in protein concentration of a transgene-encoded protein. Correction is required. See MPEP § 608.01(b).

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 15 recites the limitation "the ATP/ADP transporter" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

5. Claims 1, 4, 9-11, 13, and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a method comprising any change in distribution of ATP and/or ADP in any plant. This broad recitation encompasses use of chemical inhibitors, expression of proteins that can modulate the activity of ATP transporters, antisense-suppression of transporters, knock-outs, activation tagging, targeted mutagenesis, RNAi, ribozymes, etc.

However, the instant application has only described the use of an antisense construct comprising a potato cDNA for an ATP/ADP transporter linked in antisense orientation to the 35S promoter in transgenic potato plants (see paragraph bridging pages 3-4 and paragraph bridging pages 14-15). Claims 9-11 and 15 recite limitations that narrow the scope to reducing the activity or

concentration or expression of a protein involved in subcellular distribution of ATP and/or ADP, however, they still encompass many embodiments that have not been described in the instant application. The instant application has not provided any description of any method other than antisense for decreasing the concentration of a plastidiary ATP/ADP transporter.

The essential feature of the invention is the decrease of the plastidiary ATP/ADP transporter function which results in an increase of accumulation of a separate transgene-encoded protein. The instant specification has not described any chemical inhibitors with this function, nor has the instant specification described any materials or methods that provide this function other than an antisense construct comprising a potato cDNA for an ATP/ADP transporter.

Given the breadth of the claims which encompass a large genus of embodiments of the invention, and given only one method reduced to practice, the requirements for written description have not been met.

6. Claims 1, 4, 9-11, 13, and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing the concentration of a transgene-coded protein in a potato plant comprising transforming a potato plant with an antisense construct comprising a potato cDNA for an ATP/ADP transporter operably linked in antisense orientation to a promoter that functions in potato plants, does not reasonably provide enablement for any other method of increasing the content of a transgene-coded

biomolecule in any other organism using any other method of changing the distribution of ATP and/or ADP in cells of the organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are broadly drawn to a method comprising any change in distribution of ATP and/or ADP in any plant.

The nature of the invention is a molecular biological approach utilizing antisense to suppress the expression of the endogenous ATP/ADP transporter in the choloroplasts of potatoes. This suppression results in an increase in accumulation of a transgene-encoded protein.

The prior art teaches that antisense constructs have been successful in suppressing the expression of endogenous ATP/ADP transporters in transgenic potatoes and tobacco (see Tjaden et al. (1998) The Plant Journal, Vol. 16, pp. 531-540 and Hausler et al. (1998) Planta, Vol. 204, pp. 366-376).

The instant specification provides guidance for how to make an antisense construct comprising a cDNA from potato and how to transform a potato plant with this construct and provides this as a working example (see pages 14-15). However, the instant specification does not provide any further guidance for any method other than antisense for reducing the concentration, expression, or activity of the

ATP/ADP transporter. Nor does the specification provide any guidance for any host plant other than a potato plant.

The claims encompass the use of antisense in multiple plant species. The specification in the instant application only discloses an antisense construct comprising a potato cDNA (see paragraph bridging pages 14-15). Antisense suppression of gene expression is highly unpredictable, and the prior art suggests that success depends on the percent identity between the sequence of the antisense construct and the target gene sequence (see Elomaa et al. (1996) Molecular Breeding, Vol. 2, pp. 41-50; paragraph bridging pages 47-48, in particular). In the prior art, Klee et al. teach that antisense genes would probably be species-specific, and therefore a different antisense gene would be required for each species of plant desired to be transformed (see US Patent # 5,702,933, issued Dec. 30, 1997, column 1 lines 60-65, in particular). Both Tjaden et al. and Hausler et al. teach the use of a species-specific antisense construct (see Tjaden et al., page 532, first paragraph; and Hausler et al., page 367, second paragraph).

Because of the sequence variability between the different genes in different species of plants and because of the inconsistent results taught in the prior art, there is a high degree of unpredictability in the use of antisense to inhibit the expression of different genes. Given the breadth of the claims encompassing any method of inhibiting expression or activity of any protein involved in subcellular distribution of ATP and/or ADP in any plant, and given that there is only one

working example and a high degree of unpredictability as discussed above, it would require undue experimentation on the part of one of skill in the art to practice the method of the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 4, 9-11, 13, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Hausler et al. (Planta (1998) Vol. 204, pp. 366-376) taken with the evidence of Bevan M. (Nucleic Acids Research (1984) Vol. 12, pp. 8711-8721).

The claims are drawn to a method of increasing the content of one or more transgene-coded biomolecules, said method comprising a change in distribution of ATP and/or ADP in any plant, including decreasing the expression of an ATP/ADP transporter.

Hausler et al. teach a method of making transgenic tobacco plants comprising an antisense construct that suppresses the expression of the endogenous ATP/ADP transporter in the transformed plants (see page 368, right column). The antisense construct they utilize is in a pBIN19-based binary vector (see page 367, second paragraph), and Bevan teaches that this vector comprises the neomycin phosphotransferase gene (see page 8713, second paragraph), which encodes NPTII

and confers kanamycin resistance. Therefore, the tobacco plants transformed with the antisense construct to suppress expression of the ATP/ADP transporter that are taught by Hausler et al. are also expressing NPTII. The characteristic of having a higher accumulation of NPTII (a transgene-coded biomolecule) would be an inherent feature of these plants.

8. Claims 1, 4, 9-11, 13, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Tjaden et al. (The Plant Journal (1998) Vol. 16, pp. 531-540) taken with the evidence of Bevan M. (Nucleic Acids Research (1984) Vol. 12, pp. 8711-8721).

The claims are drawn to a method of increasing the content of one or more transgene-coded biomolecules, said method comprising a change in distribution of ATP and/or ADP in any plant, including decreasing the expression of an ATP/ADP transporter.

Tjaden et al. teach a method of making transgenic potatoes comprising an antisense construct that suppresses the expression of the endogenous ATP/ADP transporter in the transformed potatoes (see paragraph bridging pages 532-533). They also use a pBIN-based binary vector (see page 538, right column, second paragraph), and, as discussed above, this means the potato plants they produced are also expressing NPTII. The characteristic of having a higher accumulation of NPTII (a transgene-coded biomolecule) is an inherent feature of these plants.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CKW
Aug. 30, 2006

ANNE KUBELIK, PH.D.
PRIMARY EXAMINER